REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectively requested. Claims 1-7 and 9-22 were pending, of which claims 14 and 15 were withdrawn from consideration as allegedly directed to non-elected subject matter. Claims 14 and 15 have been canceled without prejudice to future prosecution in a related application. Claims 23 and 24 have been added to recite certain embodiments of the present invention. Support for these two new claims may be found, for example, at page 3, line 22, of the present application. Accordingly, claims 1-7, 9-13, and 16-24 are pending. Claims 4 and 11-13 have been amended merely for editorial purposes. No new matter has been added.

Application Status

The Action indicates that the request filed on March 1, 2004 for a Continued Prosecution Application (CPA) under 37 CFR § 1.53(b) based on parent application No. 09/800,016 is acceptable and a CPA has been established.

Applicants wish to draw the Examiner's attention to the fact that the request filed on March 1, 2004 was for a Request for Continued Examination under 37 CFR § 1.114, rather than a request for CPA. Corrections with respect to the application status are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-7, 9 and 16-22 stand under 35 U.S.C. §103(a) as being unpatentable over the LEUKINE® Sargramostim product insert, in view of Chalmers, Manufacturing Chemist & Aerosol News (March 1978, cited by Applicants), and U.S. Patent Number 5,217,954 (Foster *et al.*), and in the case of claims 4-7, further in view of U.S. Patent Number 5,545,536 (Kaushansky *et al.*), for the reasons set forth in the previous Office Action (mailed May 15, 2003). The Action deems unpersuasive the arguments in the previous response (filed on March 1, 2004) that no motivation to combine the cited references was present in prior art. The Action asserts that the motivation to combine the cited references may be found in the LEUKINE® Sargramostim product insert, which warns against administering benzyl alcohol to newborns. In addition, the Action asserts that the motivation to combine the cited references may also be

found in Foster *et al.*, which describes the use of EDTA to stabilize a cytokine (*i.e.*, bFGF) preparation.

Applicants respectfully traverse this ground of rejection. Applicants submit that a *prima facie* case of obviousness has not been established by the Action: There is not sufficient motivation for one of ordinary skill in the art to combine the cited references. The warning against administering benzyl alcohol to neonates in the LEUKINE® Sargramostim product insert does not provide the necessary motivation for substituting benzyl alcohol with EDTA in a GM-CSF formulation. First, the product insert describes not only LEUKINE formulations that contain benzyl alcohol, but also a LEUKINE formulation that does not contain benzyl alcohol. More specifically, the product insert describes that lyophilized LEUKINE may be constituted with 1 mL sterile water for injection (*see*, the second paragraph on page 1 of the insert). Thus, one of ordinary skill in the art, in view of the insert as a whole, would use lyophilized LEUKINE reconstituted in sterile water for administering to neonates. Such an approach would avoid significant time and efforts required for developing a new formulation for a limited population (*i.e.*, neonates).

Even assuming for the sake of argument that one is motivated to substitute benzyl alcohol with another antimicrobial preservative for administering GM-CSF in neonates, EDTA would not be an obvious choice. Generally, a substance must meet the requirements of appropriate regulatory guidelines regarding Antimicrobial Effectiveness Testing (AET) and Preservative Effectiveness Testing (PET) to be considered for use as a preservative. There is no evidence in the art that EDTA meets such requirements. Although the Action states that "EDTA is disclosed at the FDA website as an approved drug additive for use in solution (see http://www.accessdata.fda.gov/scripts/cder/iig/getiigWEB.cfm)," Applicants failed to identify any support for such a statement on the cited website (or other FDA databases). Should this ground of rejection be maintained, Applicants respectfully request that a paper copy of the content at the cited website be provided.

Furthermore, Applicants respectfully submit that the alleged motivation based on the warning against administering benzyl alcohol to neonates in the LEUKINE® Sargramostim product insert would not be applicable to new claims 23 and 24, which are directed to

physiologically acceptable aqueous solution of GM-CSF that comprise both EDTA and benzyl alcohol.

Applicants further submit that the Foster *et al.* reference also fails to provide the necessary motivation for using EDTA to stabilize GM-CSF. That both bFGF and GM-CSF are cytokines is insufficient for motivating one of ordinary skill in the art to stabilize GM-CSF with EDTA. The term "cytokine," as known in the art, refers to extracellular signal protein or peptide that acts as a local mediator in cell-cell communication and encompasses a diverse group of proteins and peptides with different amino acid sequences and functions. In fact, bFGF and GM-CSF are unrelated in their amino acid sequences: They only share about 10% sequence identity. As one of ordinary skill in the art would appreciate that a primary factor that determines the level of protein degradation is the amino acid sequence of the protein of interest. Accordingly, Applicants believe that such a person, in view of the sequence differences between bFGF and GM-CSF, would not have been motivated to use EDTA to stabilize GM-CSF.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

Claims 10-13 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the LEUKINE® Sargramostim product insert, Chalmers, Foster, and further in view of U.S. Patent Number 6,500,418 B1 (Dieckgraefe *et al.*) for reasons set forth in the previous Office Action mailed May 15, 2003.

Applicants respectfully traverse this ground of rejection. As discussed above, the composition of claim 1 is not obvious in view of the LEUKINE® Sargramostim product insert, Chalmers, and Foster for failing to provide the necessary motivation for using EDTA to stabilize GM-CSF. Such a deficiency has not been remedied by the Dieckgraefe *et al.* reference. More specifically, the Dieckgraefe *et al.* reference relates to the use of GM-CSF in treating inflammatory bowel disease. It does not suggest or teach the use of EDTA in stabilizing GM-CSF. Thus, Applicants submit that the methods of using the composition of claim 1, as recited in claims 10-13, would not be deemed obvious in light of the Dieckgraefe *et al.* reference.

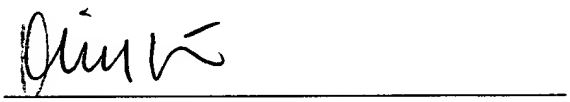
In view of the above remarks, Applicants submit that this ground of rejection has been overcome. Withdrawal of this rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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